

A Case of Onychomycosis due to *Aspergillus flavus* in all Fingernails and Toenails of an Immunocompromised Patient

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Abstract

Onychomycosis is a common disorder which is characterized with thickness and discoloration of nails. It accounts for the half of the nail disorders. Diabetic patients are particularly susceptible to fungal infections due to modifications that occur in their immunological system. Studies detected an increased risk among all three major groups of organisms that can cause onychomycosis in diabetic patients: dermatophytes, yeasts, and non-dermatophyte molds. We present a case of onychomycosis due to *Aspergillus flavus*. The patient was an immunocompromised 41-year-old male who identified with diabetes mellitus and pancreas cancer. The presence of *Aspergillus flavus* in a nail was confirmed using microscopic and culture analysis followed by Matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS). *Aspergillus flavus* have been rare reported at onychomycosis.

Keywords: Onychomycosis; *Aspergillus flavus*; Diabetes mellitus; Malignant disease

Introduction

Onychomycosis is the general name for a mycotic nail infection caused by dermatophytes, yeasts, and nondermatophyte molds. The prevalence of onychomycosis has been reported to be 2–30% and has increased in recent years [1]. The classification is; distal subungual, proximal subungual, candidal, white superficial and dystrophic onychomycosis. The aetiology of this condition is multifactorial. Old age, toenail deformities, onychodystrophy, diabetes mellitus, psoriasis, cellular immunity disorders, genetic predisposition, peripheral arterial circulatory disorder, other circulatory disorders, nail and nail fold microtrauma, and immunosuppression should be considered as risk factors for onychomycosis [2]. Three types of fungus cause onychomycosis: Dermatophytes are a homogeneous group of keratophilic fungi. The pathogen most frequently isolated from toe onychomycosis is *Trichophyton rubrum*. The majority of toenail infections are caused by dermatophytes. Yeasts are true fungi that lack hyphae and cannot therefore be classified as moulds. *Candida albicans* is the yeast most commonly isolated (5.6%). Yeasts typically affect fingernails rather than toenails. Moulds (nondermatophytic fungi) are more rarely involved and the most commonly isolated saprophytic mould is *Aspergillus* species [3].

Aspergillus species are ubiquitous environmental molds frequently isolated from soil, air, water, and vegetation. Over the recent years, onychomycosis caused by different *Aspergillus* species is increasing, evidenced by case reports and epidemiological studies [4-6]. The incidence rate of onychomycosis caused by *Aspergillus spp.* has been described as 2.6% to 6.1%, varying depending upon the reporter [7].

As in our case, the presence of immunosuppressive diseases such as diabetes mellitus and pancreatic cancer has been a predisposing factor in the development of *A. flavus*.

Case Report

41-year-old male was admitted to the dermatology outpatient clinic of our hospital with complaints of deformity and thickening of the hand nails and toe nails that had continued for nearly one year. In the dermatological examination of bilateral hand nails and toe nails, subungual hyperkeratosis in varying degrees, yellow-brown discoloration was observed (Figure 1).



Figure 1: Brown discoloration and total dystrophy on the thumb fingernails and toe nails.

The general physical examination of patient was done according to his complaints of extreme fatigue and weight loss and pain in the right upper abdomen. He had a past medical history of diabetes mellitus that was diagnosed 8 years back and the thickening of his nails has reached 1 year. He was using antidiabetic drugs. His family history consisted of diabetes mellitus and coronary artery disease.

A direct mycological examination was performed 10% potassium hydroxide preparation (KOH), and fungal structures such as arthrospores and hyphae were considered as conferring positivity in the direct examination. The patient's fingernail was planted in appropriate media. After a certain period of time the cultures of the fingernail yielded greenish-yellow to olive colored, velvety to woolly colonies. Microscopic examination of the lactophenol cotton blue stained colonies indicated long conidiophores with spherical to elongate vesicles surrounded by uniseriate phialides and conidia are globose to ellipsoidal, when assessed with colony characteristics compatible with *A. flavus*. Later on, the necessary procedures were performed on the breeding colony and identified on VITEK- MALDI-TOF MS device. Both MALDI-TOF MS and microscopy results were evaluated together the breeding colony was identified as *A. flavus* (Figure 2).

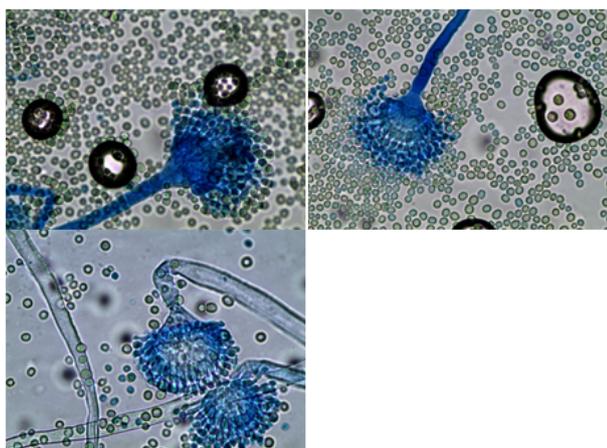


Figure 2: Slide culture shows conidial heads each consisting of a vesicle and radially arranged conidia.

Laboratory studies were obtained. Complete blood count, erythrocyte sedimentation rate, liver and kidney function tests, blood glucose, pancreas amylase, lipase levels, carcinoembryonic antigen (CEA) and lactate dehydrogenase (LDH) were within normal limits in laboratory tests. Hemoglobin: 11.78 g/dl (N 13.5-17.5 g/dl), carbohydrate antigen 19-9 (Ca 19-9) 9019 U/ml (N 0-35 U/ml).

The patient's clinical examination was found a tender mass in the upper right region. Computerized tomography of patient's upper and lower abdomen was performed. CT scan of the abdomen revealed a mass of 4.2 × 3 cm in diameter was detected in the pancreas. Sclerotic metastasis was detected in the anterior corpus of the lumbar vertebra 2. Fine needle aspiration biopsy was performed. Biopsy was compatible with pancreas end-stage adenocarcinoma.

The patient was diagnosed with pancreatic cancer and 6 cycles of chemotherapy treatment were started. In this case, the patient was

given chemotherapy with Oxaliplatin 130 mg, Irinotecan 280 mg, Fluorouracil 3790 mg and Folinic Acid 630 mg. The treatment was determined to be every 28 days. The Ca 19-9 value at the end of 2nd cycle was 1339.8. Improvement was observed in the nails during chemotherapy. At the end of the 4th month, nail development was observed in the proximal part of all nails and thinning of the nail was observed (Figure 3).



Figure 3: Patient's nails after 4 doses of chemotherapy.

Topical antifungal lotion treatment was planned after the patient was finished with chemotherapy. The chemotherapy treatment of the patient is still given in the oncology department.

Discussion

Onychomycosis is an infection of the nail plate by fungal microorganisms. This disease occurs *via* fungal invasion of the nail. Over the development course of the infection, there is initial colonisation with subsequent invasion of the nail bed and plate that cause changes in the nail colour, texture, and shape. Onychomycosis is a highly prevalent infection worldwide with a range between 2% and 30%, corresponding to 50% of nail diseases and 30% of superficial mycoses. Onychomycosis is a common nail ailment associated with significant physical and psychological morbidity [8]. A higher prevalence has been reported in men, individuals over 60 years of age, patients with immunosuppressive diseases, such as human immunodeficiency virus (HIV) infection or immunological defects, diabetics, and patients with peripheral vascular disease and malignant disease. Onychomycosis is a well-known complication of diabetes mellitus. About one third of diabetic patients are affected [9]. Studies have shown that diabetic patients are at a higher risk of contracting onychomycosis compared to non-diabetics [10]. It is caused by dermatophytes, nondermatophytic molds, and yeasts.

Although it is reported that dermatophytes and yeasts are the most common cause for onychomycosis, nondermatophyte molds (NDM) such as *Aspergillus spp.*, *Fusarium spp.*, *Acremonium spp.*, and *Scopulariopsis spp.*, were also found as the most common pathogens for onychomycosis in patients with diabetes [11]. In the past, these molds have been regarded as saprophytic or opportunistic fungi and have been basically ignored. Recently, as a consequence of an increase in the number of cases of immunodepression and environmental changes, more attention has been given to this wide, but generally non-pathogenic group of fungi [11].

Aspergillus species are a large group of common saprophytic molds which are often isolated from soil, air, and plant materials. *Aspergillus* species can cause superficial onychomycosis, distal-lateral subungual onychomycosis and proximal subungual onychomycosis. Onychomycosis due to *Aspergillus* species is rare, accounting for less than 2% of all cases [12]. Diabetes, peripheral vascular disease, trauma

and immunosuppression are the most important underlying conditions in onychomycosis due to *Aspergillus* species. *Aspergillus* species are increasingly being reported as primary causative agents of onychomycosis worldwide. Wijesuriya et al. showed that *Aspergillus* species was the most common pathogen isolated from toe nail infection [13].

MALDI-TOF MS (Matrix- assisted laser desorption ionization-time of flight mass spectrometry) is a new and sensitive method for identification of microorganisms [14]. In comparison with conventional identification methods that rely on biochemical tests and require long incubation procedures, identification by MALDI-TOF MS of microorganism is reliable and much quicker. The diagnosis of non-dermatophyte mold onychomycosis requires stringent criteria than that of dermatophytes. Because both KOH and fungal culture false negative results or long incubation time required, we used MALDI-TOF as the confirmation test.

Skin manifestations are a reflection of many of the internal diseases. Sometimes, skin disease may be the only manifestation of the internal disease. Internal malignancies may give rise to a number of cutaneous manifestations through their immunological, metabolic, and metastatic consequences. A skin finding may be an indicator of internal malignant diseases. Ductal adenocarcinoma, which represents the most common type of exocrine carcinoma, accounts for approximately 85% of pancreatic tumors, while tumors derived from the endocrine pancreas, arising from the cells of the islets, represent 5% [15,16]. Pancreatic ductal cell adenocarcinomas showing an increasing incidence in the developed countries. Factors associated with the higher incidence of pancreatic ductal cell adenocarcinoma are smoking, obesity, diet, diabetes mellitus, chronic pancreatitis, and genetic predisposition in approximately 5-10% of patients [17].

Nondermatophyte moulds (NDM) were the rare cause of onychomycosis. In our patient, malignancy and diabetes mellitus suppress the immune system and promote the development of onychomycosis in all nails.

Conflict of Interest

No conflict of interest has been reported by the authors.

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